REMARKS

I. Status of the Claims and Previous Rejections.

Claims 88 to 100 and 102 to 112 are pending in the application. Claims 88 to 100, 104, 106 to 110, and 112 have been withdrawn from consideration as drawn to non-elected species. Therefore claims 102, 103, 105, and 111 are pending and currently under examination.

Claims 88 and 102 have been amended to recite ". . . such that the secondary and tertiary structure of the self protein is essentially preserved[.]" Support for that amendment can be found in the specification as-filed, for example, at page 3, lines 26-30; and at page 4, lines 7-10. Thus the claim amendments are fully supported and add no new matter.

With respect to all claim amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to prosecute any presently excluded claim embodiments in a future continuation and/or divisional application.

Applicants gratefully acknowledge the Examiner's withdrawal of: (1) the prior rejection of claims 102, 103, 105, and 111 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement; and (2) the prior rejection of claims 102, 103, 105, and 111 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

II. Rejection under 35 U.S.C. § 112, first paragraph (Written Description).

The Examiner has rejected claims 102, 103, 105, and 111 under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. In particular, the Examiner alleged that "[t]here is no support for the recitation of 'secondary' in claim 102" and noted that the specification discloses "that the secondary and tertiary structure are preserved to a large extent." Office Action, section 2, page 2.[1] Consequently, the Examiner alleged that

[1] Claims 103, 105, and 111 all depend directly or indirectly from rejected claim 102, and therefore incorporate by reference all elements of that claim, although they do not recite the term "secondary" to which the Examiner objects. Applicants assume that claims 103, 105, and 111 have been rejected under 35 U.S.C. § 112, second paragraph for that reason, and note therefore that all arguments relating to amended claim 102 complying with the written description requirement also apply to claims 103, 105, and 111.

"[t]he disclosure provided in the specification is not commensurate in scope with the claimed invention (aka the claimed invention constitutes new matter)." *Id.*

Applicants respectfully traverse. To assess whether a claim satisfies the written description requirement, the fundamental factual inquiry "is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. MPEP § 2163.02 (citing *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)). An Applicant shows possession of the claimed invention by describing it with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Id.* (citing *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997)).

Moreover, the subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement. Nevertheless, without acquiescing to the rejection, and solely to expedite prosecution, Applicants have amended claim 102 to recite ". . . such that the secondary and tertiary structure of the self protein is essentially preserved[.]"[2] Support for that amendment can be found in the specification as-filed, for example, at page 3, lines 26-30; and at page 4, lines 7-10. Applicants believe that that amendment renders moot the rejection of claims 102, 103, 105 and 111 under 35 U.S.C. § 112, first paragraph, and therefore ask that it be withdrawn.

III. Rejection under 35 U.S.C. § 112, second paragraph (Indefiniteness).

The Examiner has rejected claims 102, 103, 105, and 111 under 35 U.S.C. § 112, second paragraph as allegedly indefinite. In particular, the Examiner alleged that the phrase "the secondary structure of the . . . self-protein is essentially preserved"[3] renders claim 102 indefinite because "it is unclear what changes to the secondary structure would or would not be

[2] Applicants have correspondingly amended withdrawn claim 88.

[3] Applicants have omitted the word "pathogenic" from this quotation because the phrase "an analog of a pathogenic self-protein" in claim 102 was amended to recite "an analog of a self-protein" in the Amendment and Response filed May 15, 2009.

encompassed by the aforementioned term."[4] Office Action, section 6, page 3. As in previous Office Actions,[5] the Examiner continues to assert that "it is unclear if this term encompasses changes at the physical/chemical level (*e.g.*, crystal structure) or simply functional changes (*e.g.*, still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen)." *Id.* For the reasons discussed below, Applicants respectfully traverse.

A. Amended claims 102, 103, 105, and 111 apprise one of ordinary skill in the art of their scope, and provide clear warning to others regarding what constitutes infringement of the patent.

When reviewing a claim for compliance with the definiteness requirement of 35 U.S.C. § 112, second paragraph, "the examiner must consider the claim as a whole to determine whether the claim apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph, by providing clear warning to others as to what constitutes infringement of the patent." MPEP § 2173.02 (citing *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000)).

Amended claim 102 complies with the definiteness requirement of 35 U.S.C. § 112, second paragraph, because one skilled in the art reading claim 102 as a whole would be apprised of its scope, and therefore serves the notice function required by statute.

Indeed, the plain language of amended claim 102 makes clear that "functional changes"—adopting the Examiner's terminology—to the secondary and tertiary structure of a self-protein analog would be encompassed by the phrase "the secondary and tertiary structure of the . . . self-protein is essentially preserved[.]" Amended claim 102 recites:

> [a] method for inducing autoantibodies against a self-protein in a subject, said method comprising:

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[4] Claims 103, 105, and 111 all depend directly or indirectly from claim 102, and therefore incorporate by reference all elements of that claim, although they do not themselves recite the phrase "the secondary structure of the . . . self-protein is essentially preserved" to which the Examiner objects. Applicants assume that claims 103, 105, and 111 have been rejected under 35 U.S.C. § 112, second paragraph for that reason, and note therefore that all arguments relating to the definiteness of amended claim 102 also apply to claims 103, 105, and 111.

[5] Applicants note that previous rejections were directed to the phrase "the tertiary structure of the . . . self-protein is essentially preserved" but based on essentially the same argument.

> administering to the subject an analog of the self-protein made by molecular biological means, wherein said analog is made by substituting one or more peptide fragments in the self-protein with a corresponding number of immunodominant foreign T-cell epitopes selected from ovalbumin, hen egg lysozyme, tetanus toxoid, or diphtheria toxoid T-cell epitopes,
>
> such that the secondary and tertiary structure of the self protein is essentially preserved; *such that said analog induces an autoantibody response as evidenced by antibody binding to the unmodified self-protein*

(emphasis added). Thus, the secondary and tertiary structure of a self-protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response in a subject; and (2) the induced autoantibodies bind to the corresponding unmodified self-protein. The plain language of claim 102 therefore apprises one skilled in the art of its scope—the secondary and tertiary structure of a self-protein is essentially preserved when those two criteria are satisfied—and thereby serves the notice function required by statute.

B. Amended claims 102, 103, 105, and 111 are definite under 35 U.S.C. § 112, second paragraph, because one of ordinary skill in the art understands what is claimed in light of the specification.

Definiteness of claim language under 35 U.S.C. § 112, second paragraph, is not analyzed in a vacuum, but in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP § 2173.02. The essential inquiry focuses upon "whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity." *Id.* Acceptability of claim language "depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification." *Id.* Accordingly, "a claim term that is not . . . defined in the specification is not indefinite if the meaning of the claim term is discernible." *Id.* (citing *Bancorp Services, L.L.C. v. Hartford Life Ins. Co.*, 359 F.3d 1367, 1372, 69 USPQ2d 1996, 1999-2000 (Fed. Cir. 2004)).

Amended claim 102 complies with the definiteness requirement of 35 U.S.C. § 112, second paragraph, because one of ordinary skill in the art understands what is claimed in light of the specification, as shown in the accompanying Declaration of Alain Delcayre under 37 C.F.R. § 1.132 ("Delcayre Declaration").

Dr. Delcayre has conducted research in the fields of vaccines and immunotherapy for more than twenty years and therefore qualifies as one of ordinary skill in the art in those fields. Delcayre Declaration, ¶¶1-2 and Exhibit 1. Based on the claim language as amended, Dr. Delcayre understands that the secondary and tertiary structure of a self-protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response in a subject; and (2) the induced autoantibodies bind to the corresponding unmodified self-protein. Delcayre Declaration, ¶¶5-6.

According to Dr. Delcayre, the content of the specification as-filed confirms that understanding. Delcayre Declaration, ¶7. For example, the specification explains that the surprising observations underlying the claimed invention resulted from the fact that various T-cell epitopes are inserted into the self-protein, "against which it is the purpose to raise antibodies." *Id.* (citing Specification as-filed, page 3, line 28). The T-cell epitopes are substituted for fragments of the self-protein having the same number of amino acids as the introduced T-cell epitope, "thus preserving the secondary and tertiary structure of the self-protein to a large extent." *Id.* (citing Specification as-filed, page 3, lines 29-30). The specification further explained that "[i]t is of importance to essentially preserve the tertiary structures, as it is done in the present invention, because these structures determine the specific recognition of the non-modified self-protein by the induced [auto-]antibodies." *Id.* (citing Specification as-filed, page 4, lines 7-10).

Furthermore, Dr. Delcayre states that one skilled in the art could easily determine whether a particular self-protein analog induces an autoantibody response in a subject, and if so, whether the induced autoantibodies bind to the corresponding unmodified self-protein using any of several common immunoassay techniques. Delcayre Declaration, ¶6. Such confirmatory assays are routine experimentation within the level of ordinary skill in the art.

Dr. Delcayre concludes that, like the amended language of claim 102, the specification makes clear that the secondary and tertiary structure of the self-protein analog is essentially preserved where: (1) the self-protein analog induces an autoantibody response; and (2) the induced autoantibodies bind to the corresponding unmodified self-protein. Delcayre Declaration, ¶7. In view of the remarks presented above and the Delcayre Declaration, Applicants

respectfully assert that claims 102, 103, 105, and 111 comply with the definiteness requirement of 35 U.S.C. § 112, second paragraph, and therefore ask that the rejection be withdrawn.

IV. Rejections under 35 U.S.C. § 103(a) (Obviousness).

B. Claim 102 over WO 92/05192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109.

The Examiner has rejected claim 102 under 35 U.S.C. § 103(a) as allegedly obvious over WO 1992/005192 ("Russell-Jones") in view of US Patent No. 5,716,596 ("Dean") and US Patent No. 5,969,109 ("Bona").

In particular, the Examiner alleged that Russell-Jones teaches "the claimed method except for the use of immunodominant foreign T cell epitopes derived from diphtheria toxoid[,]" that Bona teaches "that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity[,]" and that Dean teaches that somatostatin is a self-protein because of its recognized role in a variety of diseases. Office Action, section 8, page 5. Based on those teachings, the Examiner concluded that "it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention[,]" and that a skilled artisan would have been motivated to combine those alleged teachings to arrive at the claimed invention "because immunodominant foreign T cell epitopes derived from diphtheria toxoid were known in the art and diphtheria toxoid was already approved as a carrier for human vaccines." *Id.*

For the reasons discussed below, Applicants respectfully traverse.

1. The Examiner has not established a *prima facie* case of obviousness because the cited references do not provide a motivation to combine the prior art to achieve the claimed invention.

To reject a claim as *prima facie* obvious under 35 U.S.C. § 103(a), the Examiner must show that "a person of ordinary skill in the art would have been motivated to combine the prior art to achieve the claimed invention and that there would have been a reasonable expectation of success." MPEP § 2143 (quoting *Dystar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1360 (Fed. Cir. 2006)).[6] The Examiner has not met that burden,

[6] In response to Applicants' arguments in the Amendment and Response filed January 22, 2010, the Examiner alleged that "in the post KSR Int'l Co. v. Teleflex Inc. universe, motivation per se
(continued...)

because the cited references do not provide a motivation to combine the prior art to achieve the claimed invention.

Patents and patent applications are relevant as prior art for all they disclose, and must be considered in their entirety, including portions that would teach away from the claimed invention. MPEP § 2123 (citing *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (stating that patent references "are part of the literature of the art, relevant for all they contain")); *see also* MPEP § 2141.02(VI) (citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983)).

Applicants respectfully direct the Examiner to page 2, lines 19-37 of Russell-Jones, which asserts that "the carrier principle is an effective method of improving the efficacy of vaccines" but notes that the number of proteins accepted as potential carrier proteins for human use—including tetanus toxoid ("TT") and diphtheria toxoid ("DT")—is "relatively limited." Russell-Jones, page 2, lines 19-23. Russell-Jones further observed that the repeated use of a limited number of available carrier proteins "means that a large number of vaccine products will employ one of these proteins and multiple immunizations with products conjugated to these carriers increase the possibility that undesirable reactions to these carriers will occur." *Id.*, lines 24-29. Ultimately, Russell-Jones concluded that "there is a need for an alternative carrier to those currently used in conjugate vaccines which will obviate the immunological problems associated with these vaccines and yet retain the same immunogenicity as the vaccines presently in use or improve on it." *Id.*, lines 33-37 (emphasis added).

(...continued)
is not even required in a rejection under 35 USC 103." Office Action, section 8, page 7. The Examiner then stated that, according to *KSR*, "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." *Id.* Applicants note, however, that the Examiner has not rejected claim 102 under that rationale. Even if the Examiner had applied that rationale, however, because Russell-Jones teaches away from the use of DT conjugates or DT-derived peptides in vaccines for the reasons discussed in more detail below, Applicants respectfully assert that one of ordinary skill in the art would **not** recognize that the techniques of Russell-Jones relating to DT conjugates or DT-derived peptides could be used to improve the claimed methods.

In addition, Russell-Jones compared the ability of TraT- and DT-derived peptides and of PreS2-TraT and PreS2-DT conjugates to stimulate T-cells. Russell-Jones, page 22, line 1 to page 23, line 30; and page 26, line 2 to page 28, line 9. At the conclusion of those experiments, the authors concluded that TraT-derived peptides and TraT conjugates induced higher levels of T-cell activity than DT-derived peptides and DT conjugates. Indeed, the inventors observed that "the data indicate the superior utility" of TraT-derived peptides for use "in human vaccine formulations" compared to DT-derived peptides, and stated that "[t]he superior T-cell responses generated in response to TraT suggest[] that this protein (or one of its T-cell stimulatory sequences) may be a useful component of vaccines especially those against viral and parasitic diseases." *Id.*, page 28, lines 2-7.

Because Russell-Jones discloses that TraT conjugates and TraT-derived peptides induce a superior T-cell response compared to DT conjugates and DT-derived peptides, and that commonly-used TT and DT carriers can lead to immunological complications, Russell-Jones clearly teaches away from the use of DT conjugates or DT-derived peptides in vaccines or other immunotherapeutics. Accordingly, one of ordinary skill in the art would have no motivation to combine the disclosure of Russell-Jones with the disclosure of Dean and Bona.

Even if the disclosure of Russell-Jones provided one of ordinary skill in the art the motivation to combine its disclosure with that of Dean and Bona—which Applicants assuredly **do not** concede—the disclosure of Dean and Bona does not remedy the deficiencies of Russell-Jones. The Examiner cited Bona for allegedly teaching "that a T cell epitope can be substituted into a particular region of a target molecule wherein the T cell epitope retains immunogenicity." Office Action, section 8, page 5. Bona describes the production of chimeric antibodies (*i.e.*, non-self proteins) targeting foreign pathogens (*e.g.*, influenza virus) to which heterologous T- or B-cell epitopes have been added. Those epitopes are designed to stimulate or enhance a T- or B-cell response directed to the foreign pathogen targeted by the antibody (*e.g.*, influenza virus), rather than to break tolerance to a self-protein. *See, e.g.*, Bona, col. 20:35 to col. 21:25. The Examiner cited Dean simply for teaching that somatostatin is a self-protein because of its recognized role in a variety of diseases. Office Action, section 8, page 5. Dean describes the production of radiolabeled peptide derivatives and analogs of somatostatin for use as imaging and therapeutic agents, and does not mention vaccines at all. *See, e.g.*, Dean, col. 3:54-64.

Thus, Russell-Jones teaches away from the claimed invention because: (1) the TraT conjugates and TraT-derived peptides disclosed in Russell-Jones are clearly superior to DT conjugates and DT-derived peptides; and (2) the repeated use of a limited number of carrier proteins such as DT causes a variety of immunological problems. Because neither Dean nor Bona remedies the deficiencies of Russell-Jones, the cited references does not provide one skilled in the art the motivation to combine the teachings of Russell-Jones, Dean, and Bona to achieve the claimed invention. Consequently, the Examiner has not established a *prima facie* case of obviousness. Applicants therefore respectfully ask that the rejection of claim 102 as allegedly obvious over WO 1992/005192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109, be withdrawn.

2. The Examiner has not established a *prima facie* case of obviousness because one of ordinary skill in the art would not have a reasonable expectation of success to arrive at the claimed invention by combining the cited references.

In addition, the Examiner has not established a *prima facie* case of obviousness because none of the cited references, either alone or in combination, provides any expectation of success—much less a reasonable expectation of success as required by section 2143 of the MPEP—to arrive at the claimed invention because none of the references describes actually making and using a modified self-protein containing one or more T-cell epitopes substituted into the self-protein such that the secondary and tertiary structure of the self-protein is essentially preserved.

Thus, none of the cited references can provide any expectation that a modified self-protein made by substituting one or more peptide fragments in the self-protein with a corresponding number of immunodominant foreign T-cell epitopes would induce an autoantibody response to the unmodified self-protein as recited in the pending claims. Only Applicants' specification provides a reasonable expectation of success. For this additional reason, Applicants ask that the rejection of claim 102 under 35 U.S.C. § 103(a) be withdrawn.

3. The evidence of unexpected results is reasonably commensurate in scope with the claimed invention.

Finally, the Examiner observed that, according to MPEP § 716.02(d), "the 'objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence

is offered to support'" and alleged that the unexpected results discussed in the Amendment and Response filed January 22, 2010, and described in the specification are not commensurate in scope with the claimed invention because the pending claims encompass methods of treating humans while the experiments disclosed in the specification were performed in mice. Office Action, section 8, page 8. For the reasons set forth below, Applicants respectfully traverse.

To overcome a *prima facie* case of obviousness—which Applicants maintain the Examiner has not established in this case, for at least the reasons discussed in Section IV.A. above—rebuttal evidence of unexpected results need only be "reasonably commensurate in scope with the claimed invention." MPEP § 2145 (citing *In re Kulling*, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1058 (Fed. Cir. 1990); *In re Grasselli,* 713 F.2d 731, 743, 218 USPQ 769, 777 (Fed. Cir. 1983)).

Applicants respectfully assert that the unexpected results discussed in the Amendment and Response filed January 22, 2010, and described in the specification are reasonably commensurate in scope with the claimed invention. The murine immune system is a well-established model system for studying the human immune system. Indeed, many monoclonal antibody-based therapeutics consist of antibodies first isolated from mice and later modified, or "humanized" to reduce their immunogenicity. *See, e.g.*, Bona, col. 3:50 to col. 4:5. Furthermore, as the Examiner is undoubtedly aware, those skilled in the art routinely conduct preclinical studies of potential human therapeutics—immunomodulatory and otherwise—in a variety of mouse strains. Promising results obtained in mice frequently lead to the eventual conduct of clinical trials in humans.

Therefore Applicants respectfully assert that the mouse data presented in the specification is "sufficient to establish a reasonable correlation between the showing and the entire scope of the claim, when viewed by a skilled artisan." MPEP § 2145 (citing *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987); *Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980)). For this additional reason, Applicants ask that the rejection of claim 102 under 35 U.S.C. § 103(a) be withdrawn.

C. Claim 111 over WO 92/05192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109, further in view of WO 93/05810 and US Patent No. 5,698,195.

The Examiner has rejected claim 111 under 35 U.S.C. § 103(a) as allegedly obvious over WO 1992/005192 ("Russell-Jones") in view of US Patent No. 5,716,596 ("Dean") and US Patent No. 5,969,109 ("Bona") as applied to claim 102 above, and further in view of WO 1993/005810 ("Hellman") and US Patent No. 5,698,195 ("Le"). In particular, the Examiner asserted that the rejection of claim 102 (*see* Section IV.A. above) rendered obvious the claimed invention "except for the use of TNFα[,]" but cited Hellman for allegedly teaching that "modulation of self-proteins responsible for manifestations of a particular disease can be achieved" by eliciting antibodies to a particular self-protein by administering the self-protein conjugated to a carrier comprising a T_H-cell epitope and Le for allegedly teaching that anti-TNFα antibodies can be used to treat TNFα-mediated diseases in humans. Office Action, section 9, page 8. The Examiner therefore concluded that "[i]t would have been *prima facie*[] obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention[.]" *Id.*

Applicants respectfully traverse for at least the reasons set forth in Section IV.A. above regarding the rejection of claim 102 under 35 U.S.C. § 103(a). In addition, neither Hellman nor Le remedies the deficiencies of Russell-Jones discussed in detail above. Indeed, neither Hellman nor Le teaches or suggests substituting any of the T-cell epitopes recited in the pending claims as amended into a self-protein, or that a self-protein with a T-cell epitope substituted within it can induce an autoantibody response as shown by auto-antibody binding to the unmodified self-protein.

Consequently, the Examiner has not established a *prima facie* case of obviousness. Applicants therefore respectfully ask that the rejection of claim 111 as allegedly obvious over WO 1992/005192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109, further in view of WO 1993/005810 and US Patent No. 5,698,195 be withdrawn.

D. Claims 103 and 105 over WO 92/05192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109, further in view of US Patent Publication No. US 2003/0099634 A1.

The Examiner has rejected claims 103 and 105 under 35 U.S.C. § 103(a) as allegedly obvious over WO 1992/005192 ("Russell-Jones") in view of US Patent No. 5,716,596 ("Dean")

and US Patent No. 5,969,109 ("Bona") as applied to claim 102 above, and further in view of US Patent Publication No. US 2003/0099634 A1 ("Vitiello"). In particular, the Examiner asserted that the rejection of claim 102 (*see* Section IV.B. above) rendered obvious the claimed invention "except for use of the ovalbumin epitope recited in claim 105[,]" but cited Vitiello for allegedly teaching an immunogenic peptide comprising the ovalbumin epitope and concluded that "[i]t would have been *prima facie*[] obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention[.]" Office Action, section 10, page 9.

Applicants respectfully traverse for at least the reasons set forth in Section IV.A. above regarding the rejection of claim 102 under 35 U.S.C. § 103(a). In addition, Vitiello does not remedy the deficiencies of Russell-Jones discussed in detail above. That is, Vitiello does not teach or suggest substituting any T-cell epitope into a self-protein such that the secondary and tertiary structure of the self-protein is essentially preserved. Moreover, Vitiello does not teach or suggest substituting any of the T-cell epitopes recited in the pending claims as amended into a self-protein, or that a self-protein with a T-cell epitope substituted within it can induce an autoantibody response as shown by auto-antibody binding to the unmodified self-protein.

Consequently, the Examiner has not established a *prima facie* case of obviousness. Applicants therefore respectfully ask that the rejection of claims 103 and 105 as allegedly obvious over WO 1992/005192, in view of US Patent No. 5,716,596 and US Patent No. 5,969,109, further in view of US Patent Publication No. US 2003/0099634 A1 be withdrawn.

V. Conclusion.

In view of the amendments and remarks presented above, Applicants believe that each of the presently pending claims is in condition for allowance. Accordingly, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. If the Examiner determines that a telephone conference would expedite prosecution of this application, Applicants invite the Examiner to telephone the undersigned at the number listed below.

In the event that the United States Patent & Trademark Office ("USPTO") determines that an extension of time or other relief is required, Applicants hereby petition for any relief including extensions of time, and authorize the Commissioner of the USPTO to charge the cost

of such petitions and/or any other fees due in connection with the filing of this document to **Deposit Account No. 50-5338**, referencing **Docket No. BNIT0003-PCT-US**. However, the Commissioner is not authorized to charge the Issue Fee to the Deposit Account.

Respectfully submitted,

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